wherein, N represents a nucleotide or a non-nucleotide linker; X and Y are independently oligonucleotides of length sufficient to stably interact with a target nucleic acid molecule; Z is an oligonucleotide having a nucleotide sequence selected from the group consisting of 5'-AGAUAACGUGAAGAU-3' (SEQ ID NO 97) and 5'-AAUGGCCUAUCGGUGCGA-3' (SEQ ID NO 98); _____ represents a chemical linkage; and C, G, A, and U represent cytidine, guanosine, adenosine and uridine nucleotides, respectively.

A marked up copy of the original paragraph showing the changes made by this amendment is attached as **APPENDIX A**.

IN THE SPECIFICATION:

Please replace the paragraph found on page 4, line 7 – page 5, line 10 with the following:

In the above formulae, each N represents independently a nucleotide or a non-nucleotide linker, which may be same or different; X and Y are independently oligonucleotides of length sufficient to stably interact (*e.g.,* by forming hydrogen bonds with complementary nucleotides in the target) with a target nucleic acid molecule (the target can be an RNA, DNA or RNA/DNA mixed polymers, including polymers that may include base, sugar, and/or phosphate nucleotide modifications; such modifications are preferably naturally occurring modifications), preferably, the length of X and Y are independently between 3-20 nucleotides long, e.g., specifically, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 17, and 20); X and Y may have the same lengths or may have different lengths; m, n, o, and p are integers independently greater than or equal to 1 and preferably less than about 100, specifically 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 50; wherein if $(N)_m$ and $(N)_n$ and/or $(N)_o$ and $(N)_p$ are nucleotides, (N)m and (N)n and/or $(N)_o$ and $(N)_p$ are optionally able to interact by hydrogen bond interaction; preferably, (N)m and (N)n and/or $(N)_o$ and $(N)_p$ independently form 1, 2, 3, 4, 5, 6, 7, 8, 9 base-paired stem structures; D is U, G or A; L_1 and L_2 are independently linkers, which may be the

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same or different and which may be present or absent (*i.e.,* the molecule is assembled from two separate molecules), but when present, are nucleotide and/or non-nucleotide linkers, which may comprise a single-stranded and/or double-stranded region; _____ represents a chemical linkage (*e.g.* a phosphate ester linkage, amide linkage or others known in the art); • represents a base-pair interaction; Z is independently a nucleotide sequence selected from the group comprising 5'-AGAUAACGUGAAGAU-3' (SEQ ID NO 97) and 5'-AAUGGCCUAUCGGUGCGA-3' (SEQ ID NO 98), additions, deletions, and substitutions to these sequences may be made without significantly altering the activity of the molecules and are hence within the scope of the invention; and C, G, A, and U represent cytidine, guanosine, adenosine and uridine nucleotides, respectively. The nucleotides in each of the formulae I and II are unmodified or modified at the sugar, base, and/or phosphate as known in the art.

Please replace the paragraph on page 11, lines 26-28 with the following:

"**Figure 7** is a representative diagram of structural similarities between Class I (SEQ ID NO 117), (substrate SEQ ID NO 103) and Class VIII (SEQ ID NO 121), (substrate SEQ ID NO 103) enzymatic nucleic acid molecules of the invention."

Please replace the paragraph on page 39, lines 2-15 with the following:

"The initial population of RNA for *in vitro* selection was created by first generating a double-stranded DNA template for *in vitro* transcription. SuperScript® II reverse transcriptase (RT, GibcoBRL) was used to extend 280 pmoles of the DNA oligonucleotide "primer 1" (5′-GAAATAAACTCGCTTGGAGTAACCATCAGG-ACAGCGACCGTA-3') (SEQ ID NO 99); region representing 16 possible nearest neighbor combinations is underlined) using 270 pmoles of the template DNA (5′-TCTAATACGACTCACTATAGGAAGACGTAGCCAAN$_{40}$TACGGTCGCTGTCC TG-3') (SEQ ID NO 100); T7 promoter is underlined and N represents an equal

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A4 cont'd

mixture of the four standard nucleotides). The extension reaction was conducted in a total of 50 µl containing 50 mM Tris-HCl (pH 8.3 at 23°C), 75 mM KCl, 3 mM $MgCl_2$, 10 mM dithiothreitol (DTT), 0.2 mM each of the four deoxyribonucleoside-5′ triphosphates (dNTPs), and 10 U μl^{-1} RT by incubation at 37°C for 1 hr. The resulting double-stranded DNA was precipitated by the addition of 5 µl 3 M sodium acetate (pH 5.5) and 140 µl 100% ethanol and pelleted by centrifugation. This extension reaction provides ~10^{14} different template sequences."

Please replace the paragraph on page 39, line 27 – page 40, line 10 with the following:

A5 amendment

"The initial selection reaction (G0) contained 2000 pmoles of RNA in a total of 400 µl reaction buffer (50 mM HEPES [pH 7.5 at 23°C], 250 mM KCl and 20 mM $MgCl_2$) and was incubated at 23°C for 4 hr. The reaction was terminated by the addition of EDTA and the RNA was recovered by precipitation with ethanol. RNA cleavage products were separated by denaturing 10% PAGE, visualized and quantified using a Molecular Dynamics PhosphorImager®, and the gel region corresponding to the location of the desired RNA cleavage products was excised. The RNA was recovered from the excised gel by crush-soak elution followed by precipitation with ethanol. The selected RNAs were amplified by RT-PCR as described previously (10) using primers 1 and 2 (5′-GAATTCTAATACGACTCACTATAGGAA-GACGTAGCCAA-3') (SEQ ID NO 101); T7 promoter is underlined). The resulting double-stranded DNA from each round of *in vitro* selection was used to transcribe the RNA population for the subsequent round, in which all steps were conducted at ~1/10^{th} the scale of G0. All other parameters of the selection process were maintained as in G0. Representative ribozymes from the populations derived from 6, 9, 12 and 15 rounds of selection were examined by cloning (TOPO®-TA cloning kit; Invitrogen) and sequencing (ThermoSequenase® kit; Amersham Pharmacia)."

A marked up copy of the original paragraph showing the changes made by this amendment is attached as **APPENDIX B**.

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IN THE TABLES:

Please replace the originally filed Tables VII and VIII (pages 53-55, as filed), with substitute Tables VII-VIII (pages 53-55), submitted herewith.

THE SEQUENCE LISTING:

Please incorporate the sequence listing submitted herewith on paper into the application after the Abstract (page 62), in compliance with CFR § 1.77(b). The sequence listing is submitted herewith in CRF format (3.5" disk) and on paper, in compliance with 37 CFR §§ 1.821-1.825.

The sequences in the sequence listing are consistent with those found in the amended specification, Tables, and Figures, submitted herewith, and do not constitute new matter.

IN THE FIGURES:

Please replace Figures 1-7, with substitute Figures 1-7, submitted herewith.

A marked up copy of the original Figures 1-7 showing changes made by this amendment is attached as **APPENDIX C**.

REMARKS

Claims

Claim 2 has been amended only by changing the SEQ ID NO used to identify the sequences contained in the claim so that they conform with the amendments to the Tables, specification, Figures, and the sequence listing submitted herewith. This amendment has not been made for any reason related to patentability, and does not constitute new matter. A copy of the marked up original claim 2 showing changes made by this amendment is attached as **Appendix A**.

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